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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/019,494

03/08/2002

Samuel D. Bernal

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1407

24574 7590 10/18/2007
JEFFER, MANGELS, BUTLER & MARMARO, LLP
1900 AVENUE OF THE STARS, 7TH FLOOR
LOS ANGELES, CA 90067

EXAMINER

EBRAHIM, NABILA G

ART UNIT	PAPER NUMBER
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1618

MAIL DATE	DELIVERY MODE
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10/18/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/019,494

Applicant(s)

BERNAL ET AL.

Examiner

Nabila G. Ebrahim

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 August 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 is/are pending in the application.
- 4a) Of the above claim(s) 2 and 11-20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>8/7/07</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Receipt of Applicant's remarks, amendments and Information Disclosure Statement to the claims dated 8/7/07 is acknowledged.

Status of Claims

Claims 1, 2, 11-20 are pending in the application.

Claims 3-10 were previously cancelled.

Claims 2, and 11-20 were withdrawn from consideration.

Status of Office Action: Final.

The rejections that are not reiterated in this office action are withdrawn.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the

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applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Pomerantz Edwin WO 9726018 (Pomerantz) in view of Oseroff et al., Intramitochondrial Dyes Allow Selective in vitro Photolysis of Carcinoma Cells, PNAS, December 15, 1986, vol. 83, no. 24, 9729-9733 (hereinafter Oseroff) Copyright © 1986 by the National Academy of Sciences.

Pomerantz teaches in vivo detection (corresponds to step b of claim 1) of oral premalignant lesions and oral carcinomas, including the steps of sequentially rinsing (corresponds to step a of claim 1) the oral cavity with a dye stain composition which is selectively retained by cancerous and precancerous tissues, and a rinse composition for removing unretained stain composition, the step of applying to oral tissue, a stain composition comprising a non-toxic dye other than toluidine blue 0 (claim 1). Pomerantz also disclosed that this type of staining is dependent on the dye gaining access to internal subcellular structures such as the nucleus. Such access is readily obtained only by "fixing" a tissue sample of formaldehyde or other reagent that disrupts the cellular membrane without destroying general cellular structure (page 2, line 26 bridging to page 3, line 4). Note that it is expected that the mitochondria as a subcellular structure would at least partially absorb the dye. It is also known that the disclosure of oral carcinomas means oral malignancy of epithelial cells recited in instant claim 1.

In addition, Pomerantz teaches that in-vivo diagnostic procedures for detection of premalignant oral lesions or oral carcinomas, employing dye compositions, which are selectively retained by tissues rendered abnormal due to dysplasia, hyperplasia, tumorigenesis, and other active surface lesions, are known in the art.

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Pomerantz did not teach explicitly that the mitochondria is the subcellular structure that will be marked by the dye. Further Pomerantz did not disclose the specific agents recited in claim 1 as amended.

Oseroff teaches that carcinoma cell mitochondria preferentially accumulate and retain cationic dyes to a much greater extent than most normal cells. In addition, Oseroff teaches that rhodamine and cyanine dyes were tested because they can potentially serve as targets for highly selective photochemotherapy. It is noted that alcian blue dye recited by Applicant in amended claim1 is a cationic cyanine dye.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use a non-toxic dye other than toluidine blue 0 to mark premalignant carcinoma cells as Pomerantz teaches to target the mitochondria that will be marked because Oseroff teaches that mitochondria in carcinomatous cells can absorb cationic dyes to a much greater extent than normal cells. The claim would have been obvious because a person of ordinary skill has good reason to pursue the known options within his grasp, the skilled artisan would have a good reason in Oseroff's research to navigate between different cationic cyanine dyes that can detect oral epithelial carcinoma using the method taught by Pomerantz since it would lead to the anticipated success, it is likely that the results that have been reached are not of innovation but of ordinary skill and common sense. The expected result would be a method to detect cancerous cells of the oral epithelium in vivo.

Response to Arguments

Applicant's arguments filed 8/6/07 have been fully considered but they are not persuasive. Applicant argues that:

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1. Pomerantz does not disclose selective marking of the mitochondria.

To respond: Pomerantz combined with Oseroff disclose the same method using similar dyes to detect the same pathological cells in the same site (oral epithelium) and Oseroff discloses literally the selectiveness in the mechanism. Oseroff recites literally the selective marking of mitochondria.

2. There is no disclosure in Pomerantz of agents selected from the group consisting of alcian blue, malachite green, phenosafranin, acriflavine, pyronine Y, toluylene blue, brilliant green, peonidin, oxythiamine, tiemunium iodide, elliptinium acetate, or furazolium chloride.

To respond: as explained above Oseroff teaches that cyanine dyes can be used as intramitochondrial dyes to allow selective in vitro photolysis of carcinoma cells. It is noted that alcian blue is a cyanine dye and that a person of ordinary skill has good reason to pursue the known options within his grasp according to Oseroff's research to navigate between different cationic cyanine dyes that can detect oral epithelial carcinoma using the method taught by Pomerantz since it would lead to the anticipated success.

Conclusion

3. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the

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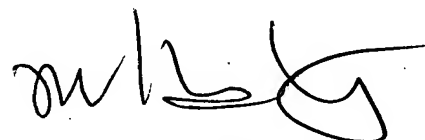
extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nabila G. Ebrahim whose telephone number is 571-272-8151. The examiner can normally be reached on 8:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nabila Ebrahim
10/13/07

A handwritten signature in black ink, appearing to read 'Michael G. Hartley', with a stylized flourish at the end.

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER